

Kidney Transplantation: Success Breeds Failure

The last decade in nephrology has seen increasing attention to the care of patients with chronic kidney disease (CKD). The development and implementation of practice guidelines such as the Kidney Disease Outcomes Quality Initiative have led to more extensive research into the pathophysiology, consequences, and treatment of the complications of CKD. Patients with progressive stage 3 and 4 now have blood pressure control, diabetes, anemia, secondary hyperparathyroidism, nutrition, metabolic acidosis, and cardiovascular disease much more aggressively monitored and treated. It is now hard for me to believe that as an internal medicine intern in 1990, I was taught (by physicians who participated in the clinical trials that later disproved the hypotheses) that treatment in the elderly of systolic blood pressures of 160 was controversial and that control of diabetes improved maternal-fetal outcome but not nephropathy. The recently reported decline in incidence of end-stage renal disease from the National Institutes of Health may indeed be a positive reflection of this change.

A second concomitant trend, as discussed by Dr Daniel Brennan in this issue, is the vast improvement in short-term outcomes in kidney transplantation despite a lagging improvement in long term outcomes. Acute rejection, including those episodes attributed to nonadherence, at most centers is in the single digits, cytomegalovirus infections are now routinely prevented and treated with outpatient oral medications, and lower corticosteroid dosing in the first year has led to less wound healing, infectious, and musculoskeletal complications. Furthermore, improvement in diagnostic and surgical techniques has improved the immediate morbidity of kidney transplantation; the average initial hospitalization is now less than 1 week. This has a 2-fold effect: other problems are now more prominent (eg, polyoma virus, humoral rejection, calcineurin inhibitor toxicity, and so on) and that slow progressive loss of kidney function without a major heralding event (i.e. CKD) is now the predominant form of transplant failure. Lastly, in the new CKD staging system adopted by the Centers for Medicare and Medicaid Services this year, a perfect kidney trans-

plant would only transform a stage 5 CKD patient into a stage 2 or 3 CKD patient.

These advances and the subsequent new problems have posed difficulties to the transplant community. When and how aggressively should allograft dysfunction be evaluated and treated? When should a patient be referred for a second kidney transplant? Who should be responsible for the standard CKD care, the transplant team or the referring nephrologists? Are the complications and treatment of CKD in the transplant population the same as in the general population? This issue attempts to begin to answer some of these tough questions. However, initial and anecdotal reports suggest that CKD care given to transplant patients is worse than the general CKD population and that the initial morbidity and mortality of transplant patients who return to dialysis are greater than any other similar cohort.

An additional problem is that most major transplant clinical trials are based on short-term results or use clinical surrogate end points to mimic long term results. The "hard" endpoints in recent prospective CKD trials (eg, death, dialysis, or transplantation) have for the most part only been evaluated in retrospective database analyses. Furthermore, with less than 15,000 transplants performed in the United States and most centers performing less than 100 transplants annually, it will be difficult to power "hard" endpoint trials adequately, even if the investigators at each transplant center, stubborn and notorious for idiosyncratic policies, can agree on standard treatment protocols, particularly with immunosuppression.

Thus, a paradigm shift is underway. Similar to the experience of transplant cardiologists who spend much of their time treating heart failure and transplant hepatologists who spend much of their time treating cirrhosis, kidney transplant professionals will spend much of their professional time managing CKD. Let's hope we are up to the challenge.

Brent W. Miller, MD
Guest Editor

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